Remarks

This Application is currently under Final Rejection. Claims 14-16 and 20-25 currently stand allowed. Claims 6-9 currently stand objected to as being dependent from a rejected claim. Claims 1-5, 10, 17, 18, and 26-29 currently stand rejected. Applicants request continued examination under 37 C.F.R. 1.114.

Please note that Claims 1, 10, 20, 26, and 28 have been amended in part to bring them into uniformity with the Preliminary Amendment, adding further definition of the terms substituted phenyl, heteroaryl, etc., which prior amendment was inadvertently omitted in Applicants last listing of the Claims. Claims 1, 10, 20, 26, and 28, have been further amended to more particularly claim preferred compounds of the present invention. No new matter is added.

Claim 28 (and presumably Claim 29 dependent thereon) currently stands rejected under the argument that the term "neuronal protein extravasation" renders the claim indefinite. Applicants renew their assertion that those skilled in the art would have no trouble understanding the meaning of this term as used in the specification and claims and recognizing that such extravasation is an abnormal physiological condition that can cause undesirable symptoms, as for example but not limited to migraine, as discussed in the specification and the previously submitted references. (See also Moskowitz, reference CE of Form 1449, 2nd and 3rd paragraphs). Applicants acknowledge their prior oversight that the exact term "neuronal protein extravasation" is not found in the references, but are reminded that an Applicant can be their own lexicographer in drafting a specification and assert that the terms "dural protein extravasation" (Journal of Neuroscience Methods, vol. 81 (1998), pg. 19, last sentence of the first paragraph), "protein extravasation" in reference to quantification of neurogenic dural inflammation (Ibid. first sentence of the second paragraph), "dural extravasation" (Ibid. pg. 20, line 4), "plasma protein extravasation in the dura" (NeuroReport 8, pg. 2237 (1997), and "dural plasma protein extravasation" (Ibid. pg 2238, lines 21-22), are all synonymous with "neuronal protein extravasation" as used in the present specification and claims, and that such meaning would be clear to those skilled in this art. Therefore, neither the term nor the Claim is indefinite. Withdrawal of the rejection is respectfully requested.

Claims 17-18 currently stand rejected under 35 U.S.C. 112, 2nd paragraph, under

the assertion that the term nitronium ion lacks antecedent basis. Though applicant respectfully disagrees with this view for the reasons previously stated, in an effort to facilitate allowance, the Claims have been amended to obviate the rejection without changing the scope of the subject matter claimed. Withdrawal of the rejection is respectfully requested.

Claims 1,2,4,5,10, and 26-29 currently stand rejected under 35 U.S.C 103(a) as being obvious over Carr. Claims 1-5, 10, and 26-29 currently stand rejected under 35 U.S.C 103(a) as being obvious over Butera, Oinuma, or Helsley, alone or in view of Carr. Applicants respectfully traverse.

Carr discloses a class of piperidinyl compounds including benzoylpiperidines useful as Class III antiarrhythmic agents and 5-HT_2 antagonists. Though a floating valence in the general formula for Carr may allow substituent NHY to be at the 3 position (meta), as in the presently claimed compounds, ALL exemplified compounds are only substituted at the 4 position (para), as acknowledged by the Examiner. It is noted that Carr does not teach or suggest 5-HT_{1F} agonists.

Butera discloses another class of compounds including benzoyl-tetrahydropyridine/piperizines useful as Class III antiarrhythmic agents which have alkylsulfonamido or arylsulfonamido substituents in the para position of the phenyl ring. It is noted that the compounds disclosed in Butera are not piperidinyl compounds as the presently claimed compounds, and that Butera does not teach or suggest 5-HT_{1F} agonists.

Oinuma discloses another class of compounds useful as tranquilizers, antihypertensives, and analgesics, which do not have the R^1 substituents on the phenyl ring as in the presently claimed invention. It is noted that Oinuma also does not teach or suggest 5-HT_{1F} agonists.

Helsley discloses another class of compounds useful as Class III antiarrhythmic agents which have alkylsulfonamido or arylsulfonamido substituents in the para position of the phenyl ring. It is noted that Oinuma does not teach or suggest 5-HT_{1F} agonists.

It is submitted that a prima facia case for obviousness has not, in fact been made out. Therefore no showing against specific compounds in the cited references is

necessary and the previously submitted declaration can be used as persuasive evidence for that purpose. M.P.E.P §2144.09, first paragraph states,

> A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities **and similar utilities**. 'An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, **in the expectation that compounds similar in structure will have similar properties**.' *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA) 1979)."

(emphasis added). The section goes on to explain in the 11-13th paragraphs that:

> The presumption of obviousness based on a reference disclosing structurally similar compounds may be **overcome where there is evidence showing there is no reasonable expectation of similar properties in structurally similar compounds.** *In re May* ,574 F.2d 1082,197 USPQ 601 (CCPA 1978)(appellant produced sufficient evidence to establish a substantial degree of unpredictability in the pertinent art area, and thereby rebutted the presumption that structurally similar compounds have similar properties); *In re Schechter*, 205 F.2d 185,98 USPQ 144 (CCPA 1953). See also *Ex parte Blattner*, 2 USPQ2d 2047 (Bd.Pat. App.&Inter.1987)(Claims directed to compounds containing a 7-membered ring were rejected as *prima facie* obvious over a reference which taught 5-and 6-membered ring homologs of the claimed compounds. The Board reversed the rejection because the prior art taught that the compounds containing a 5-membered ring possessed the opposite utility of the compounds containing the 6-membered ring, undermining the examiner's asserted *prima facie* case arising from an expectation of similar results in the claimed compounds which contain a 7-membered ring.).
>
> **If the prior art does not teach any specific or significant utility for the disclosed compounds,then the prior art is not sufficient to render structurally similar claims *prima facie* obvious** because there is no motivation for one of ordinary skill in the art to make the reference compounds, much less any structurally related compounds. *In re Stemniski* ,444 F.2d 581, 170 USPQ 343 (CCPA 1971). Where structurally similar "prior art compounds 'cannot be regarded as useful ' for the sole use disclosed [by the reference],...a person having ordinary skill in the art would lack the 'necessary impetus 'to make the claimed compounds. "*In re Albrecht*, 514 F.2d 1389,1396,185 USPQ 585,590 (CCPA 1975)(prior art reference studied the local anesthetic activity of various compounds, structurally similar to those claimed were irritating to human skin and therefore "cannot be regarded as useful anesthetics." 514 F.2d at 1393,185 USPQ at 587).

> Similarly, **if the prior art merely discloses compounds as intermediates in the production of a final product, one of ordinary skill in the art would not have been motivated to stop the reference synthesis and investigate the intermediate compounds with an expectation of arriving at claimed compounds which have different uses**. *In re Lalu* ,747 F.2d 703, 223 USPQ 1257 (Fed.Cir.1984).

(emphasis added).

None of the cited references teach or suggest the referenced compounds have 5-HT_{1F} agonist activity. Applicants have previously submitted a declaration showing how alteration of the R^1 substituent at the 3-position (meta) to the 4-position (para) of the phenyl ring destroys the desired 5-HT_{1F} activity, thereby persuasively demonstrating a substantial degree of unpredictability in the pertinent art area. It is not necessary that the comparator compounds be contained within the cited references, only that the showing demonstrate unpredictability in structurally similar compounds. This declaration is, therefore, sufficient to rebut the presumption that structurally similar compounds have similar properties, particularly in that the structural change demonstrated to cause the unpredictability in the desired activity is the structural change at issue in the proposed *prima facie* obviousness case.

Further, as stated in the cited M.P.E.P section, disclosed intermediates without teaching of the desired utility do not render structurally similar compounds claimed for specific utilities *prima facie* obvious.

For these reasons, Applicants assert that there is no prima facie case for a rejection under 35 U.S.C. 103. Withdrawal of the rejection is respectfully requested.

Applicants believe all rejections and objections to the present application have been overcome and that the application is in condition for allowance. Reconsideration and timely issuance of a notice of acceptance is respectfully requested.

The Examiner is kindly invited to telephone the below signed attorney if there are any further issues or questions regarding this application if such could facilitate the allowance of this case.

Respectfully submitted,

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